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(71) Applicant *(for all designated States except US)*: BIOSENSE INC. [US/US]; Suite 10, 40 Ramland Road South, Orangeburg, NY 10962 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: BEN-HAIM, Shlomo [IL/IL]; 101 Yefe-Nof Street, 34454 Haifa (IL).

(74) Agents: COLB, Sanford, T. et al.; Sanford T. Colb & Company, P.O. Box 2273, 76122 Rehovot (IL).

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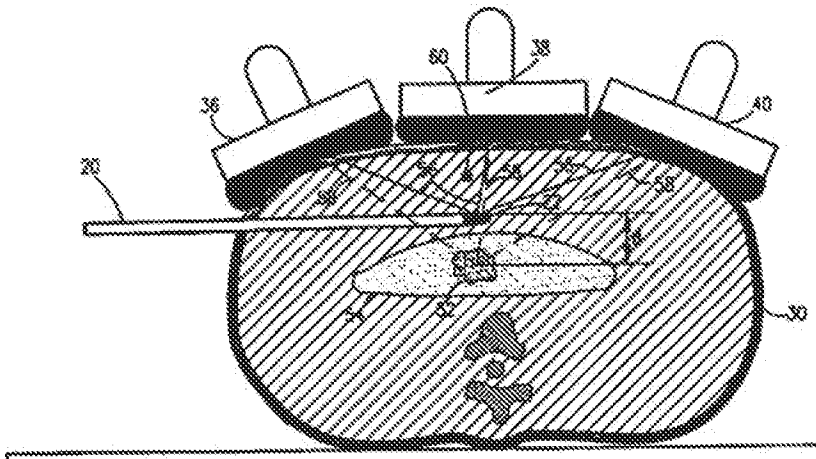

(57) Abstract

A method for optimizing irradiation of a moving target area (52) inside the body of a subject (30), including: providing a probe (20) inside the body, so that a sensing portion (22) of the probe (20) is inside or adjacent to the moving target area (52); generating one or more radiation fields in a vicinity of the moving target area (52); measuring a physical parameter related to the radiation fields at the sensing portion (22) of the probe (20); and adjusting at least one of the radiation fields in response to the physical parameter measurement. The radiation fields are adjusted by adjusting the orientation, position, power level and/or direction of at least one radiator (36, 38, 40) that generates one of the radiation fields.

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INTRABODY ENERGY FOCUSING

RELATED APPLICATIONS

This application claims the priority of the following U.S.. Provisional patent applications: "Catheter Based Surgery", No. 60/011,721, Filed February 15, 1996 and "Lesion Locating Method", No. 60/012,275, filed February 26, 1996. This application is also related to the following PCT applications, filed on even date as the instant application by applicant Biosense Inc., all of which applications designate, *inter alia*, the U.S.: "Catheter Based Surgery" and "Locatable Biopsy Needle", both of which were filed in the Israeli receiving office and "Medical Procedures and Apparatus using Intrabody Probes", filed in the U.S. receiving Office. The disclosures of all the above applications are incorporated herein by reference. This application is also related to a PCT application titled "Multi-Element Energy Focusing", filed on even date in the Israeli receiving office, by applicant Victor Spivak.

FIELD OF THE INVENTION

The present invention relates generally to medical therapeutic systems, and specifically to systems for therapeutic irradiation of parts of the body.

BACKGROUND OF THE INVENTION

Irradiation of internal portions and organs of the body, using electromagnetic or ultrasonic radiation, is well known, for a variety of therapeutic purposes. Some representative examples include gamma-irradiation of tumors, RF hyperthermia therapy, and ultrasonic lithotripsy of kidney stones.

Typically one or more radiation sources are placed outside the patient's body and are aimed at appropriate points on the surface of the patient's body, so that the radiation they emit will pass through the desired target area or organ inside the body. In order to maximize the therapeutic effect of the radiation on a target organ or area, while reducing undesirable radiation effects on surrounding tissues, the radiation sources are frequently aimed toward the target from different angles relative to the body. Treatment personnel use various methods of radiation planning to optimize the positions and orientations of radiators used for this purpose.

Accurate radiation planning in this and other methods of radiation therapy is hampered by refraction and scattering of the radiation by body tissues, particularly in ultrasound therapy. When multiple radiators are used simultaneously, interference among the radiator beams can

also cause deviation of radiation intensity on the target inside the body from the desired level. Because of anatomical variations from patient to patient, it is difficult to predict a priori the actual intensities and relative phase angles of one or more beams of radiation that will impinge on a target area inside the body due to a given arrangement of radiators outside the body.

U.S. Patent 5,419,327 to Rohwedder et al., the disclosure of which is incorporated herein by reference, describes a acoustic therapy apparatus where reflections of a shock-wave from a calculus are used to aim subsequent shockwaves, so that the future shockwaves hit the calculus.

U.S. Patent 4,893,624 to Lele, the disclosure of which is incorporated herein by reference, describes an ultrasound hyperthermia system having a two-dimensional array of transducers and an individual lens for each transducer to aim the focal point of ultrasonic radiation emitted from that transducer.

U.S. Patent 5,415,175 to Hanafy et al., the disclosure of which is incorporated herein by reference, describes a one-dimensional array of transducers in which each individual transducer has a non-planar face.

U.S. Patent 5,045,746 to Wersing et al., the disclosure of which is incorporated herein by reference, describes a one-dimensional array of transducers in which each transducer has a trapezoidal shape.

U.S. Patent 5,526,814 to Cline et al., the disclosure of which is incorporated herein by reference, describes an ultrasonic hyperthermia system in which the focal point is aimed using a magnetic resonance imaging (MRI) system which detects the location of a hot-spot created by the hyperthermia system. The focal location may also be calculated (based on a measured position of an ultrasonic transducer) and overlaid on an MRI image. The orientation and position of the transducer may be controlled by a computer, based on a target area marked by an operator on the image.

U.S. Patent 4,620,546 to Aida et al., the disclosure of which is incorporated herein by reference, describes an ultrasonic hyperthermia system having an imaging transducer and a hyperthermia transducer. The relative positions of the two transducers are determined by a computer and the location of the focal area of the hyperthermia transducer is either calculated from the position data of the hyperthermia transducer or from reflections from the tissue at the

focal area. A symbol designating the focal area is superimposed on an image acquired by the imaging transducer.

U.S. Patent 5,113,864 to Hagmann, the disclosure of which is incorporated herein by reference, describes an RF hyperthermia system using a temperature probe adapted to being inserted into a tumor to guide the focusing of an hyperthermia RF array.

PCT publication WO 95/14505, the disclosure of which is incorporated herein by reference, describes an RF hyperthermia system in which the focusing of the system is guided using radiation probes outside of a body and inside of it.

SUMMARY OF THE INVENTION

It is, therefore, an object of the present invention to provide a method for accurately determining the intensity of radiation impinging on a target inside the body.

In one aspect of the present invention, determination of radiation intensity on the target is used in finding optimal positions, orientations and/or phases of radiators placed outside the body for purposes of radiation therapy.

In a further object of the present invention apparatus is provided for determining the intensity of radiation impinging on a target inside the body.

In preferred embodiments of the present invention, a radiation-measuring sensor is fixed adjacent to the distal end (or a sensing portion) of a probe for insertion into the body. In some embodiments of the invention, the sensors are not at a distal end of the probe, for example, when the probe is an implantable probe. The probe is inserted into the body so that its distal end is located inside or adjacent to a target area in the body. The probe sensor provides signals indicative of the radiation intensity in the target area.

Furthermore, in preferred embodiments of the present invention, one or more radiators are positioned in proximity to the body. Driver circuitry drives the radiators to emit radiation directed toward the target area. The intensity of radiation at the probe is measured by the sensor, and one or more characteristics of the radiators are adjusted so as to bring the measured intensity to a desired value.

Preferably this desired value is a maximum value of intensity measured at the target for a given, constant level of total irradiation power emitted by the one or more radiators. In this context, the total irradiation power is the sum of the irradiation powers of all of the radiators being driven.

In some preferred embodiments of the present invention, the characteristics of the radiators that are adjusted include positions and orientations thereof.

In some preferred embodiments of the present invention, such as those using two or more radiators, the characteristics of the radiators are adjusted to include the respective phases and/or frequencies of electrical signals driving the radiators and/or their positions and/or their orientation or the radiation direction of the radiator.

Preferably the phases are adjusted so as to enhance constructive interference of multiple radiator beams at the target, and/or prevent destructive interference effects at the target.

Alternatively, the frequencies are adjusted so as to prevent destructive interference effects, by driving two or more of the radiators at different frequencies.

In preferred embodiments of the present invention, the total irradiation power during the adjustment of the radiators is maintained at an initial level, which is substantially lower than a therapeutic level of total irradiation power. After the adjustment has been completed, the total irradiation power is increased from the initial level to the therapeutic level, so as to impart a desired therapeutic radiation dose to the target.

In some preferred embodiments of the present invention, the probe is inserted into the body so that its distal end is located adjacent to the target area, at a known displacement therefrom. Preferably the displacement is verified by X-ray, ultrasound, endoscopy or other imaging methods known in the art. After the characteristics of the radiators have been adjusted so as to bring the intensity measured by the probe sensor to the desired value, the characteristics are then readjusted by a known amount, for example by rotating the radiators by a known angle, calculated to bring the intensity of radiation impinging on the target to a value substantially equal to the intensity that was measured by the probe sensor.

In some preferred embodiments of the present invention, the radiator control circuitry controls the radiators dynamically during therapeutic irradiation, so as to maintain the radiation intensity on the target at a desired (therapeutic) value, despite movement of the patient or of the patient's internal organs. Preferably the radiators are adjusted to initial positions, orientations and/or phases as described above. Radiator control circuitry then adjusts the characteristics of the radiators in response to changes in the intensity and/or phase

of radiation measured by the probe, so as to maintain the measured intensity at the desired level.

In some preferred embodiments of the present invention, useful in radiation therapy of the chest and abdomen, the radiator control circuitry adjusts the characteristics of the radiators in response to positional changes of the radiator and/or a target area as the patient's chest and abdomen move due to breathing.

In other preferred embodiments of the present invention, useful in radiation therapy of the heart, the radiator control circuitry adjusts the characteristics of the radiators in response to positional changes of a target area and/or the radiator as the patient's heart moves in the cardiac cycle.

In still other preferred embodiments of the present invention, useful in radiation therapy of the gastrointestinal tract, the radiator control circuitry adjusts the characteristics of the radiators in response to changes due to peristaltic motion of the digestive organs.

In some preferred embodiments of the present invention, measurements by the probe sensor are correlated with information provided by other physiological sensors relating to the cyclical physiological motion, and the radiator control circuitry adjusts the characteristics of the radiators cyclically in response to the motion.

Thus, for example, in a preferred embodiment of the present invention, respiratory motion of the thorax and abdomen is measured by a respiration sensor, such as a bioimpedance sensor, or other types of sensors known in the art. For each of two or more points in the respiratory cycle, as determined by the respiration sensor, measurements by the probe sensor are used to determine a respective adjustment setting of the characteristics of the radiators. Preferably the total irradiation is maintained at a relatively low, initial level during this process of adjustment, as described above. After adjustment has been completed, the total irradiation is increased to the therapeutic level. Radiator control circuitry then adjusts the characteristics of the radiators cyclically during the respiration cycle between the appropriate, respective adjustment settings, in response to signals from the respiration sensor.

Preferably the radiator control circuitry adjusts the characteristics gradually, so that the radiator position, orientations and/or phases are swept gradually from one adjustment setting to the next.

In an alternative preferred embodiment of the present invention, an adjustment setting of the radiator characteristics is determined for a selected portion of the respiratory cycle during which thoracic volume is approximately constant. For example, the adjustment setting may be determined for the portion of the respiratory cycle following exhalation, during which thoracic volume is at a minimum, and whose duration is typically 30-40% of the duration of the entire cycle. A respiration sensor, as described above, is used to monitor the respiration cycle and determine, during each respiratory cycle, when the selected portion is reached. The radiators are maintained at the adjustment setting determined for this portion. The total irradiation is controlled cyclically so as to provide a relatively high, therapeutic, level of irradiation power during the selected portion of the respiratory cycle and to provide a low level of irradiation, or no irradiation, during other portions of the cycle.

In preferred embodiments of the present invention, the one or more radiators are ultrasonic radiators. Preferably, the sensor comprises an ultrasound transducer that measures the amplitude and phase of ultrasound waves impinging thereon. The radiators and sensor may be of any suitable type known in the art.

In other preferred embodiments of the present invention, the radiators are electromagnetic radiators, which emit radio-frequency radiation, and the sensor measures the amplitude and phase of electromagnetic waves. The radiators and sensor may be of any suitable type known in the art.

In some preferred embodiments of the present invention, the ultrasonic radiators or electromagnetic radiators comprise one or more steerable arrays, as are known in the art, which are controlled to direct a steerable beam of radiation emitted thereby toward the target. The steerable arrays may be of any type known in the art, including electronically-steerable phased arrays, or mechanically-steered arrays.

In still other preferred embodiments of the present invention, the radiators emit ionizing radiation, such as gamma radiation or other types of high-energy radiation known in the art, and the sensor measures the intensity of this radiation. The radiators and sensor may be of any suitable type known in the art.

In other preferred embodiments of the present invention, useful particularly in hyperthermic therapies, for example, the probe includes a thermal sensor, such as a thermistor or other temperature-sensing device known in the art, which measures the temperature at or

adjacent to the target. Preferably the positions, orientations, phases and/or irradiation power levels of the radiators are adjusted and maintained at a therapeutic level until a desired temperature at the target has been reached and/or maintained for a predetermined period of time.

In one such preferred embodiment, the probe further includes a radiation sensor, for example for measurement of ionizing radiation. Preferably the target area is first heated, for example by ultrasound or microwave irradiation. When a desired temperature has been reached, preferably 42-45°C, one or more sources of ionizing radiation irradiate the target with ionizing radiation. It has been found that heating the target in accordance with this method enhances the effectiveness of the ionizing radiation in treating cancers, for example.

As can be appreciated, a single probe may include a first sensor, such as an ultrasound radiation sensor, to guide the localized heating and a second sensor, such as an ionizing radiation sensor to guide the therapeutic radiation. Preferably, the probe includes a temperature sensor.

There is therefore provided, in accordance with a preferred embodiment of the present invention, a method for optimizing irradiation of a moving target area inside the body of a subject, including:

providing a probe inside the body, such that at least a sensing portion thereof is inside or adjacent to the moving target area;

generating one or more radiation fields in a vicinity of the target area;

measuring a physical parameter related to the radiation fields at the sensing portion of the probe; and

adjusting at least one of the radiation fields in response to the physical parameter measurement.

Preferably, adjusting at least one of the radiation fields includes adjusting an orientation and/or a position of a radiator that generates one of the one or more radiation fields.

Additionally or alternatively, adjusting at least one of the radiation fields includes varying a power level of the radiation field.

Preferably, generating one or more radiation fields includes generating a directional beam of radiation, and adjusting at least one of the radiation fields includes adjusting the direction of the directional beam of radiation.

Preferably, the radiation field is adjusted so as to maximize the intensity of radiation in the target area.

Preferably, at least two radiation fields are generated, and adjusting at least one of the radiation fields includes aiming the radiation fields commonly at the target area.

In preferred embodiments of the present invention in which the at least two radiation fields have a common frequency, adjusting at least one of the radiation fields preferably includes adjusting a phase thereof.

Preferably, measuring a physical parameter at the sensing portion of the probe includes measuring a phase of at least one radiation field thereat and/or measuring the intensity of radiation thereat.

Preferably, providing a probe in the body includes inserting the probe so that its sensing portion is located adjacent to the target area, and a displacement of the sensing portion of the probe relative to the target area is determined. Preferably, the adjustment of the radiation fields is altered in response to the displacement of the sensing portion of the probe from the target area.

Preferably, adjusting at least one of the radiation fields includes dynamically adjusting the radiation field in response to a physiological motion, and in a preferred embodiment of the invention, includes cyclically varying the radiation field between two or more adjustment settings in response to a cyclical physiological motion. The method preferably additionally includes receiving signals indicative of the physiological motion. Preferably, cyclically varying comprises applying irradiation substantially only at a portion of the physiological motion.

Preferably, dynamically adjusting the radiation field in response to a physiological motion includes dynamically adjusting the radiation field in response to respiratory motion and/or to cardiac motion and/or to gastrointestinal motion.

Preferably, generating one or more radiation fields includes generating a field of ultrasound radiation. Alternatively or additionally, generating one or more radiation fields includes generating a field of electromagnetic radiation and/or a field of ionizing radiation.

Preferably, measuring a physical parameter at the sensing portion of the probe includes measuring a temperature thereat, and adjusting at least one of the radiation fields includes reducing a power level of at least one of the one or more radiation fields when a desired

temperature is reached, and/or increasing a power level of a field of ionizing radiation when a desired temperature is reached.

In some preferred embodiments of the present invention, the method described above includes injecting a therapeutic substance, preferably microbubbles, into the target area.

Preferably, providing a probe, includes inserting a probe into the body; and maintaining the probe inside the body for at least two consecutive radiation therapy sessions.

There is also provided in accordance with a preferred embodiment of the invention, a method of optimizing irradiation of a moving target area inside the body of a subject, including,

providing a probe inside the body, such that at least a sensing portion thereof is inside or adjacent to the moving target area;

generating one or more radiation fields in a vicinity of the moving target area;

determining a relative orientation between said fields and said probe; and

adjusting at least one of the radiation fields in response to said determined relative orientation.

Preferably, adjusting at least one of the radiation fields comprises adjusting an intensity of the field.

There is further provided, in accordance with a preferred embodiment of the present invention, apparatus for irradiation of a target inside the body of a subject, including:

a probe, having a sensor at a sensing portion thereof, which is inserted into the body to a position in or adjacent to the target; and

one or more radiators, which generate energy fields in the body in the vicinity of the target,

wherein the sensor measures a physical parameter associated with the energy fields generated by the one or more radiators, and

wherein at least one of the one or more radiators has one or more adjustable characteristics, and

wherein at least one of the one or more adjustable characteristics of at least one of the one or more radiators is adjusted in response to a signal generated by the sensor.

Preferably, the sensor includes an ultrasound transducer, or alternatively, an electromagnetic sensor, an ionizing radiation sensor or a temperature sensor.

Preferably, the probe includes a lumen, which is used to convey a therapeutic substance into the body.

Preferably, the one or more adjustable characteristics include the position and/or orientation of the at least one radiator and/or the phase and/or power level of radiation generated thereby.

Preferably, at least one of the one or more radiators generates a directional beam of radiation, and the one or more adjustable characteristics include the direction of the directional beam of radiation generated by the radiator.

Preferably, the apparatus further includes a radiator controller, which adjusts at least one of the one or more adjustable characteristics automatically, and preferably dynamically, in response to motion of the target relative to the one or more radiators.

Preferably, the apparatus includes a physiological sensor, which generates signals indicative of physiological motion, which signals are received by the radiator controller.

Preferably, the one or more radiators include an ultrasound radiator and/or an electromagnetic radiator. Preferably, the one or more radiators include a phased array.

Alternatively or additionally, the one or more radiators may include a source of ionizing radiation and/or a mechanically steerable radiator.

Preferably, the apparatus is used in accordance with the method for optimizing irradiation described above.

There is therefore provided, in accordance with a preferred embodiment of the invention, a method of minimizing radiation damage to sensitive tissue during radiation therapy of a target tissue, including:

determining the position of a probe inserted in a first tissue portion, which first tissue portion has a positional relationship to the sensitive tissue, wherein the position is determined utilizing a position sensor mounted on the probe; and

determining an irradiation path from at least one radiator to the sensitive tissue responsive to the determined position and the positional relationship and responsive to an desired irradiation of the target tissue.

Preferably, the method includes adjusting an output parameter of said at least one radiator responsive to said determined irradiation path. Additionally or alternatively, the method is practiced while the first tissue is in physiological motion. Additionally or

alternatively the method includes moving said radiator relative to the first tissue. Additionally or alternatively, the sensitive tissue has a known positional relationship to the target tissue.

There is further provided in accordance with a preferred embodiment of the invention, a method for aiming a plurality of radiators at a target area inside the body of a subject, including:

providing a probe inside the body, such that at least a sensing portion thereof is inside or adjacent to the target area;

generating one or more radiation fields in a vicinity of the target area, using at least one of said plurality of radiators;

measuring a phase of said radiation fields at the sensing portion of the probe; and

repeating generating and measuring at least a second time, using at least a second one of said plurality of radiators.

Preferably, the method includes irradiating the target area using said plurality of radiators, responsive to said determined phases. Alternatively or additionally, the method includes determining the position of the sensing portion of the probe utilizing a position sensor mounted on the probe. Additionally or alternatively, repeating said generating includes repeating said generating at least two hundred times. Preferably, repeating said generating includes repeating said generating at least two thousand times.

There is further provided in accordance with a preferred embodiment of the invention, an ultrasonic radiator array including a plurality of individually controlled transducers, wherein each transducer emits an ultrasonic beam formed to have significant overlap with beams emitted by other transducers of the plurality of transducers and wherein each transducer includes a beam forming element for increasing the overlap of the beam with other beams.

Preferably, the beam forming element is integral to the transducer. Alternatively, the beam forming element is a lens.

In a preferred embodiment of the invention, the beam is defocused. Alternatively, the beam is out-of-focus.

Alternatively or additionally, the array is operative to generate an ultrasonic beam having a defined focal point. Preferably, the individual transducers are controllable to move the focal point in any direction in space.

Alternatively or additionally, the array includes an ultrasonic sensor adapted to be

inserted at a target area and a controller which aims the array in response to signal generated by the ultrasonic sensor. Preferably, the controller individually energizes each transducer and receives a signal indicative of a phase measured by the ultrasonic sensor for each such energization.

In a preferred embodiment of the invention, each transducer is at least 2.5x2.5 millimeters in dimension. Additionally or alternatively, the array is a two-dimensional array.

The present invention will be more fully understood from the following detailed description of the preferred embodiments thereof, taken together with the drawings in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic representation of a probe, in accordance with a preferred embodiment of the present invention;

Fig. 2 is a schematic illustration of a system for radiation therapy, to which methods in accordance with preferred embodiments of the present invention are applied;

Fig. 3 is a schematic cross-section of the abdomen of a patient, to which methods in accordance with preferred embodiments of the present invention are applied;

Figs. 4A and 4B are schematic cross-sections of the thorax of a patient, shown at different, respective points in the respiratory cycle, to which methods in accordance with preferred embodiments of the present invention are applied;

Figs. 5A and 5B show the relative angular extent of ultrasonic beams emitted by large and small ultrasonic transducers, respectively; and

Figs. 5C and 5D show preferred embodiments of the invention for emitting an ultrasonic beam with a relatively large angular extent from a large ultrasonic transducer.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

U.S. provisional patent application no. 60/011721, "Catheter-Based Surgery," filed February 15, 1996 and a PCT application of like title filed on even date as the instant application, both assigned to the assignee of the present application, and whose disclosures are incorporated herein by reference, describes a system for ultrasound radiation therapy useful, for example, in treating tumors located inside the body. A tumor is impregnated with microbubbles, and a target area of the body, containing the tumor, is then irradiated by intense

ultrasound radiation from one or more radiation sources. The ultrasound waves rapidly heat the microbubbles, causing them to explode and destroy surrounding tumor tissue.

Fig. 1 shows a probe 20 for insertion into the body of a subject, in accordance with a preferred embodiment of the present invention. Probe 20 as shown is a rigid catheter, of a type known in the art, which is preferably inserted surgically into the body so that the probe's distal end is positioned in or adjacent to a target area for radiation therapy. Alternatively, probe 20 may be a flexible catheter, which may be inserted into the body through a blood vessel, or it may be another type of invasive probe, as is known in the art. Preferably probe 20 also includes a lumen 27. Probe 20 may also include an endoscope or other minimally invasive probes as known in the art.

Preferably probe 20 comprises metallic or other radio-opaque material, so that its position in the body may be verified by X-ray imaging. Other methods of imaging known in the art, such as ultrasound or endoscopic imaging, may also be used for this purpose. Alternatively or additionally, probe 20 may include a position-sensing device 21, such as electromagnetic position determination devices disclosed in U.S. patent 5,391,199, to Ben-Haim, and PCT patent application number PCT/US95/01103, filed January 24, 1995, now published as WO96/05768, which are assigned to the assignee of the present application and whose disclosures are incorporated herein by reference, or other devices known in the art.

As shown in Fig. 1, sensor 22 is fixed adjacent to the distal end of probe 20. In one preferred embodiment of the invention, sensor 22 is a miniature ultrasound transducer, of a type known in the art, which generates voltage signals responsive to the amplitude of ultrasound waves impinging thereon. These signals are conveyed by wires 24 to signal processing unit 26 outside the body.

In the preferred embodiment of the present invention shown in Fig. 1, unit 26 includes a waveform display 28, which displays the amplitude of signals received from sensor 22 as a function of time, and enables an operator to observe changes in the amplitude and phase of the signals in the course of adjusting radiators used in the radiation therapy, as will be described below.

In other preferred embodiments of the present invention, unit 26 is designed to analyze the signals automatically, for example using devices and methods of frequency and phase

analysis known in the art, and to output amplitude, frequency and phase data derived therefrom.

Fig. 2 schematically illustrates the use of probe 20 in an ultrasound therapy procedure, in accordance with preferred embodiments of the present invention. A patient 30 is shown lying on an operating table 32, and probe 20 is percutaneously inserted so that its distal end is located in a tumor 34. Ultrasonic radiators 36, 38 and 40, of types known in the art, are adjustably mounted to a mounting arm 42, and are directionally adjusted so as to irradiate the area of tumor 34. Alternatively, directional adjustment of the radiators may be accomplished by means of internal aiming mechanisms, known in the art. Radiators 36, 38 and 40 and patient 30 may be immersed in a water bath (not shown), as well known in the art, or they may be coupled to the patient using a coupling gel. A radiator driver console 44 includes driver and control circuitry for driving the radiators, along with user controls 46 and a display 48. In a preferred embodiment of the invention, radiators 36, 38 and 40 are all driven to emit radiation at substantially the same frequency.

It will be appreciated that many of the principles of the present invention described here with reference to ultrasonic radiators 36, 38 and 40 can be equally applied to other radiation therapy systems, for example using RF radiators instead of ultrasound.

Although the present invention allows improved aiming of the radiators at a target inside the body, and therefore may reduce the need for additional radiation-responsive therapies, in an alternative embodiment of the present invention, microbubbles are injected through lumen 27 into tumor 34, and are heated to explosion due to irradiation by radiators 36, 38 and 40, in accordance with the above-mentioned provisional patent application no. 60/011721. Other types of heat- and/or radiation-responsive therapeutic substances may similarly be injected and used in conjunction with the system shown in Fig. 2.

In accordance with preferred embodiments of the present invention, preferably, before the optional injecting of microbubbles, and before activating all three radiators 36, 38 and 40 at full therapeutic power levels, console 44 is set to drive the radiators at lower intensities, so as to allow their orientations and phases to be adjusted. First, each of radiators 36, 38 and 40 is activated in turn, and its orientation or direction is adjusted so as to maximize the radiation intensity measured by sensor 22. Preferably, the phase of radiation emitted by each of the radiators is adjusted against a common reference, so as to cause the respective radiation fields

generated by the radiators at sensor 22 to be substantially in phase with one another. Then all three radiators are activated, and the driver and control circuitry of console 44 is preferably readjusted as necessary. As is known in the art, when all the fields are in phase at sensor 22, the radiation intensity in the target area adjacent to the probe will be maximized, due to constructive interference, while intensity in other area of the body will be lower. Thus, the therapeutic effect of the radiation on tumor 34 can be maximized, while limiting the damage to other tissues due to unwanted irradiation.

After the orientations and phases of radiators 36, 38 and 40 have been adjusted, the radiation intensity due to the three radiators is preferably measured by sensor 22, so as to calibrate the driver and control circuitry so that a desired intensity of radiation may be generated by the radiators in the target area. The patient is then prepared for radiation therapy, for example by injection of microbubbles or a heat-activated chemical agent into tumor 34, and the circuitry is adjusted and activated so as to drive the radiators to give a desired dose of therapeutic radiation, of an appropriate intensity and duration.

Alternatively, in other preferred embodiments of the present invention, when interference among the fields of radiators 36, 38 and 40 is not desired, console 44 is adjusted so as to drive each of the radiators at a different frequency. In this case, the method described above may be used to adjust the orientations and/or positions of the radiators, and calibrate the driver and control circuitry, but adjustment of the phases is not performed.

Adjustment of the radiators and console circuitry in accordance with the methods described above may be performed manually by an operator of the system shown in Fig. 2. Alternatively, in preferred embodiments of the present invention, console 44 receives outputs directly from signal processing unit 26, and then automatically adjusts the positions and/or orientations of the radiators, as well as the phases and/or frequencies at which the radiators are driven, for example, using the same methodology as described above for manual calibration.

Although for simplicity of illustration, preferred embodiments of the present invention are described with reference to an array of three radiators, it will be appreciated that the methods and inventive principles of the present invention are equally applicable to radiator arrays comprising two, four or more radiators, or an NxM matrix of radiators. Similarly, preferred embodiments of the present invention may be described with reference to a single radiator, which irradiates a target area in the body from a plurality of different positions in

succession. Multiple direction irradiation is particularly useful in ultrasonic irradiation, where bones or air spaces in the body may block ultrasonic waves from reaching part of the target area from a particular direction.

While Fig. 1 shows probe 20 inserted inside tumor 34, in some cases, it may be impractical or undesirable to insert a probe directly into the target area for irradiation. Therefore, in some preferred embodiments of the present invention, the probe is inserted to a known position adjacent to the target area, at a known displacement therefrom. Imaging methods, such as X-ray, ultrasound or endoscopic imaging, and/or position determination devices, as described above, are preferably used to determine the displacement of the probe from the target area.

Thus, as shown in Fig. 3, in a preferred embodiment of the present invention, probe 20 is inserted into the abdominal cavity of a patient 30 at a small distance anterior to the patient's liver 54, which contains a tumor 52 to be treated by ultrasound hyperthermic therapy, for example. Probe 20 includes an ultrasound sensor 22 adjacent to its distal end. An ultrasound imaging system (not shown in the figures), as known in the art, is used to observe the position of probe 20 relative to tumor 52 and to determine an approximate vector displacement, $\vec{d}$, of the probe from the tumor.

After probe 20 has been inserted and its position determined, radiators 36, 38 and 40 are aimed generally toward the probe and driven to irradiate the area of the probe at a low, initial power level. As described above, the radiators' characteristics are adjusted to give a maximal value of intensity at the probe, as measured by sensor 22. This adjustment is shown schematically by solid lines 56 in Fig. 3. Characteristics of the radiators, for example, their angular orientations and phases, are then readjusted to compensate for the known displacement $\vec{d}$, so as give a maximal value of intensity substantially in the area of tumor 52, as indicated schematically by dashed lines 58 in Fig. 3.

In some cases, refraction of the radiation, particularly ultrasound radiation, by physiological tissues introduces difficulty and, potentially, inaccuracy in determining how far to readjust the characteristics of the radiators to compensate for displacement $\vec{d}$. Therefore, in some preferred embodiments of the present invention, a calibration function is determined, by inserting probe 20, or a second, similar probe, at another known point 60 in the abdominal cavity, as shown in Fig. 3. The characteristics of radiators 36, 38 and 40 are readjusted to give

a maximal value of intensity at point 60. The known displacement of point 60 relative to the initial position of probe 20, together with the required readjustments determined as described above, are used to estimate with greater accuracy the readjustments needed to give a maximal value of intensity in the area of tumor 52.

In a preferred embodiment of the invention, irradiating a target tissue is achieved by controlling an array of ultrasonic transducers to generate a beam of ultrasound which is focused at the target tissue. Preferably, the array is an NxM rectangular array of transducers. Preferably, the irradiation frequency is about 700 kHz, which allows the focal size of the beam to be about 2-3 cubic millimeters. For this focal size many individually controlled transducers may be needed, preferably, a few hundred, more preferably, at least a thousand.

Preferably, the focal point of the beam may be moved in three dimensions. To achieve this aim using a phased array of ultrasonic transducers, the beams generated by individual transducers are required to have a considerable overlap. In general, if each individual transducer is small, it emits a wide beam. Fig. 5B shows overlapping beams emitted by adjacent small transducers 74 and 76. However, the energy level attainable by such a transducer is limited by the material strength of the transducer. In addition, using a large array having many thousands of transducers is problematic, since each transducer must be individually controlled. If each individual transducer is large the beam emitted by the transducers is narrow and there may not be sufficient overlap between beams of adjacent transducers so the array can act as a phased array. Fig. 5B shows non-overlapping beams emitted by adjacent large transducers 70 and 72.

In a preferred embodiment of the invention, large transducers are modified so they emit beams with a large angular extent. Fig. 5C shows a first such preferred embodiment, where a transducer 78 (and 80) has a focusing lens 82 (and 84) formed as an integral part thereof. If the focal length of lens 82 (and 84) is sufficiently short, the beams emitted by individual transducers, such as transducers 78 and 80, diverge and overlap.

Fig. 5D shows another preferred embodiment of the invention, where large transducers are modified to emit beams with a large angular extent. Fig. 5D shows such an embodiment where a defocusing lens 90 (and 92) is formed at the end of transducers 86 (and 88).

As can be appreciated, lenses 82, 84, 90 and 92 may be formed on the transducers themselves or, in an alternative preferred embodiment of the invention, the lens may be a lens formed of acoustically conducting material.

In a preferred embodiment of the invention, each ultrasonic transducer is 1 mm thick and 2.5x2.5 mm in profile. In a preferred embodiment of the invention, each transducer has a profile area of at least 1 mm^2. Preferably, the profile area is between 1 and 4 mm^2. Optionally, the profile area is between 4 and 9 mm^2. Further optionally, the profile area is greater than 9 mm^2, preferably at least 16 mm^2. The transducer array is preferably formed of 60x60 such elements. In a preferred embodiment of the invention, the array is formed of between 200 and 600 elements. Optionally, the array is formed of between 600 and 3000 elements. Further optionally, the array is formed of between 3000 and 6000 elements. Preferably, each element is individually controllable, alternatively, groups of elements may be controlled together when lower resolution/ faster response is required.

Such a focused array may be used for localized heating, tissue destruction or shock-wave therapy. Alternatively or additionally, the array is used for imaging, preferably, 3D scanning of tissue volumes. Preferably, the same array being used for imaging as for ultrasonic irradiation. Thus, propagation path errors are reduced. Where necessary, multiple arrays may be positioned around a patient and individually controlled to focus on target tissues. Such arrays may be smaller than a single large array and still irradiate the target tissue with a similar (total) amount of energy.

If an especially precise focusing of ultrasonic energy is desired, probe 20 may be brought into the location to be irradiated for determining the setup of the transducer array to focus energy at sensor 22. Probe 20 is then moved out the irradiation location so that the tissue enters the volume previously taken up by probe 20. When the energy is radiated at the tissue, the volume previously occupied by sensor 22 is focal point of large amounts of energy. Alternatively, an antenna (not shown) is attached to sensor 22. The antenna is preferably smaller than probe 20, so it can enter an irradiation volume without substantially affecting the tissue location. Thus, irradiation levels can be monitored during the irradiation itself, even when the focal size is smaller than probe 20. Such an antenna may be made of an acoustically conducting material (for ultrasound irradiation) or the antenna may be a microwave antenna

(for microwave irradiation). Alternatively, the focal size of the array is made larger than the tip of probe 20, so that sensor 22 can monitor actual energy levels delivered to the tissue.

Although the above preferred embodiments have been described with reference to ultrasonic irradiation of a target area in the body, in other preferred embodiments of the present invention, the radiators are electromagnetic radiators, which emit radio-frequency radiation, and the sensor measures the amplitude and phase of electromagnetic waves. The radiators and sensor may be of any suitable type known in the art, for example, electromagnetic coils.

In still other preferred embodiments of the present invention, the radiators emit ionizing radiation, such as gamma radiation, X-rays or other types of high-energy radiation known in the art, and the sensor measures the intensity of this radiation. The radiators and sensor may likewise be of any suitable type known in the art, for example X-ray tube radiators and a solid-state radiation detector.

In some preferred embodiments of the present invention, radiators 36, 38 and 40 comprise phased arrays of radiator elements, as are known in the art, for example, phased arrays of ultrasound transducers or of RF antenna elements. Phased arrays generate relatively narrow, directional beams of radiation, whose direction, intensity and phase may be controlled and varied by radiator control circuitry in control console 44, shown in Fig. 1. It will be appreciated that such phased arrays are particularly useful in conjunction with the present invention, because of the relative ease and accuracy with which they may be adjusted to give a maximal value of intensity on the target.

In other preferred embodiments of the present invention, radiators 36, 38 and 40 comprise mechanically-steerable radiator elements or mechanically steerable arrays of radiator elements, as are known in the art. Such steerable elements or arrays generate directional beams of radiation, whose direction, intensity and phase may be controlled and varied by radiator control circuitry in control console 44. It will be appreciated that such steerable elements or arrays, like phased arrays, are particularly useful in conjunction with the present invention, because of the relative ease and accuracy with which they may be adjusted to give a maximal value of intensity on the target.

Figs. 4A and 4B show another preferred embodiment of the invention, in which radiators, preferably phased arrays, are adjusted dynamically during irradiation, so as to

maintain the radiation intensity on the target at a desired value, despite movement of the patient and/or the patient's internal organs. Probe 20, having sensor 22 adjacent to its distal end, is inserted into target area 34 in the thoracic cavity 60 of patient 30, as described above. As shown in Fig. 4A, radiators 36, 38 and 40 are controlled by radiator control circuitry 61, which adjusts the beam directions of the radiators as indicated by dashed lines 62, so as to give a maximal value of intensity on target 34 when the thoracic cavity is expanded to its maximal volume, at the peak of inhalation.

As shown in Fig. 4B, however, when the patient exhales, thoracic volume decreases, and the adjustment illustrated by dashed lines 62 in Fig. 4A no longer gives the maximal value of intensity on target 34. At the point of minimal thoracic volume, i.e., full exhalation, the beam directions of radiators 36, 38 and 40 must be readjusted, as indicated by solid lines 64, to give the maximal value of intensity on target.

In a preferred embodiment of the present invention, radiator control circuitry 61 varies the adjustment of radiators 36, 38 and 40 between the directions indicated by dashed lines 62 and those indicated by solid lines 64 in response to changes in thoracic volume as patient 30 breathes. Preferably the adjustment is varied smoothly between the two extreme settings illustrated by lines 62 and 64 respectively, so that the radiation intensity on target 34 is at a nearly maximal value during all portions of the respiratory cycle. Additional adjustment settings in between the two extremes may also be determined and used by the radiator control circuitry, if desired, in order to maintain a more nearly maximal value of intensity on target 34 during intermediate portions of the cycle.

In the preferred embodiment of the present invention shown in Figs. 4A and 4B, radiator control circuitry 61 receives respiration signals from a respiration monitor 66, and uses these signals to synchronize the adjustment of radiators 36, 38 and 40 with the respiratory cycle, as described above. Respiration monitor 66 may be a bioimpedance monitor, as is known in the art, which receives and analyzes electrical signals indicative of expansion and contraction of the thorax from chest electrodes 68, but other respiration monitors known in the art may similarly be used.

As noted earlier, in the above preferred embodiments, described with reference to Figs. 4A and 4B, radiators 36, 38 and 40 preferably comprise steerable radiator elements or arrays, such as phased arrays or mechanically-steerable elements or arrays, whose beam directions

may be conveniently and rapidly varied. In other preferred embodiments of the present invention, using other types of radiators, however, it may be difficult or impossible to dynamically adjust radiator characteristics, such as the radiators' positions and orientations, that determine the beam directions.

Thus, in one such preferred embodiment of the present invention, which may be readily understood by reference to Fig. 4B, radiators 36, 38 and 40 are adjusted as indicated by solid lines 64, so as to give a maximal value of intensity on target 34 when thoracic cavity 60 is at or near its minimum volume, i.e., immediately following exhalation. Radiator control circuitry 61 drives radiators 36, 38 and 40 to emit intense radiation, at a therapeutic level of irradiation power, only when the thoracic cavity has contracted to a volume at or near this minimum. Preferably, the radiator control circuitry determines when to drive the radiators to emit intense radiation based on signals from respiration monitor 66, indicating when the minimum thoracic volume has been substantially reached.

Alternatively, radiator control circuitry 61 may drive radiators 36, 38 and 40 constantly at a low, initial level of irradiation. When the intensity measured by probe sensor 22 at target 34 reaches a desired value, preferably the maximal value for the initial level of irradiation, radiator control circuitry 61 drives the radiators to emit intense radiation, at a therapeutic level of irradiation power. Thus, although thoracic cavity 60 is constantly irradiated by radiators 36, 38 and 40, the radiators are driven to emit intense radiation only in a restricted period around the point in the respiratory cycle for which the radiators are adjusted to deliver maximal radiation to the target.

Although the above preferred embodiments have been described with reference to adjustment of the radiator characteristics in response to respiratory motion, the inventive principles of these embodiments may be similarly applied to synchronize irradiation with and/or adjust for other modes of physiological motion.

Thus, for example, in other preferred embodiments of the present invention, useful in radiation therapy of the heart, the radiator control circuitry adjusts the characteristics of the radiators in response to movement of the patient's heart in the cardiac cycle. The radiator control circuitry may further receive signals from an ECG monitor or other monitors of cardiac activity known in the art, and use these signals to synchronize irradiation with the heart's motion.

In still other preferred embodiments of the present invention, useful in radiation therapy of the gastrointestinal tract, the radiator control circuitry adjusts the characteristics of the radiators in response to changes due to peristaltic motion of the digestive organs.

In other preferred embodiments of the present invention, useful particularly in hyperthermic therapies, for example, the probe includes a thermal sensor 19 (shown in Fig. 1), such as a thermistor or other temperature-sensing device known in the art, which measures the temperature at or adjacent to the target. Preferably the positions, orientations, phases and/or irradiation power levels of the radiators are adjusted and maintained at a therapeutic level until a desired temperature at the target has been reached and/or maintained for a predetermined period of time.

In one such preferred embodiment, the probe further includes a radiation sensor 23 (shown in Fig. 1), for example for measurement of ionizing radiation, for controlling ionizing-radiation radiators. Preferably the target area is first heated, for example by ultrasound or microwave irradiation. When a desired temperature has been reached, preferably 42-45°C, one or more radiators are driven to irradiate the target with ionizing radiation. It has been found that heating the target in accordance with this method enhances the effectiveness of the ionizing radiation in treating cancers, for example.

In another preferred embodiment of the invention, probe 20 includes a real-time position determining means so that the radiator control circuit can track the location of probe 20. Several different embodiments are within the scope of the invention. In one embodiment, particularly suitable for x-ray and gamma-ray irradiation, the radiators comprise an omnidirectional radiation source and an aperture through which a narrow beam of radiation is actually emitted. The radiation emitting apertures of the radiators track probe 20 so as to deliver a radiation dose to the target tissue for the entire length of the cycle. This may be accomplished by reorienting the radiation apertures in real time. In a further preferred embodiment of the invention, this entire process of irradiation and reorientation of the apertures is combined with a rotation of the radiation source around the patient. Thus, the radiation dose to healthy tissue is evenly distributed so as to lessen its effect. Alternatively or additionally, the radiator control circuit incorporates a "map" of sensitive tissues which are to receive less than an equal share of radiation. The radiator control circuit preferably determines the path of radiation from the source to probe 20 (or to the target tissue, if the probe is offset

from the target tissue). If sensitive tissues lay along the path, the radiator control circuit may momentarily block (or deactivate) the radiation source, so as to lessen the radiation dose to sensitive tissues.

In some embodiments of the invention, realigning the line-of-sight of the radiation source may not be simple. For example in ultrasound radiation treatment systems, the line of sight is greatly affected by the type of tissue in the beam path. In one preferred embodiment of the invention, calibration data for the radiators is acquired at one position of probe 20, for example, end of exhalation. The radiators are then operated only when probe 20 is at or relatively near that position. It should be understood that the position of probe 20 may be acquired as an absolute position or as a position of probe 20 relative to a reference position of the patient. Thus, if the patient moves, the radiation therapy system can be reoriented to correct for gross patient movement. Alternatively, calibration data for the radiators are acquired at a multiplicity of probe positions. The driving scheme of the radiators can be determined in real time from the set of calibration data based on the position of probe 20, for example, using a look-up table. In general, movement of probe 20 is used in some preferred embodiments of the invention to determine movement of the target tissue. In some embodiments of the invention where probe 20 includes a position sensor, it is not necessary for probe 20 to include a radiation sensor. For example, in gamma-ray irradiation, the irradiated area can be determined with high precision using geometric calculations, so no radiation sensor is necessary to aim the radiators, only a position sensor.

Another benefit of using a probe with a position determination means is that the probe may be inserted into the body of a patient and to the target tissue under the guidance of a CT image on which the probe position is overlaid. Many radiation therapy systems include some type of imaging subsystem to ensure accurate aiming of the radiation beams.

Another aspect of some embodiments of the present invention relates to sensor 22. Sensor 22 may be a radiation sensor which is connected to the radiator control circuit by wire or optical cable. Alternatively, sensor 22 is a wireless sensor which is implanted at the target tissue. Thus, some embodiments of the present invention may be practiced with a minimum amount of invasiveness and without requiring catheterization of a patient each time radiation therapy is performed on the patient. A wireless sensor may be locally energized or may be energized from an outside source, such as RF radiation. Alternatively, sensor 22 may be a

transducer which emits a signal responsive to energy impinging on sensor 22. Further alternatively, sensor 22 is a reflector which reflects impinging energy to another sensor outside the patient.

It will be appreciated that the preferred embodiments described above are cited by way of example, and the full scope of the invention is limited only by the claims which follow.

CLAIMS

1. A method for optimizing irradiation of a moving target area inside the body of a subject, comprising:

providing a probe inside the body, such that at least a sensing portion thereof is inside or adjacent to the moving target area;

generating one or more radiation fields in a vicinity of the moving target area;

measuring a physical parameter related to the radiation fields at the sensing portion of the probe; and

adjusting at least one of the radiation fields in response to said physical parameter measurement.

2. A method in accordance with claim 1, wherein adjusting at least one of the radiation fields comprises adjusting an orientation of a radiator that generates one of the one or more radiation fields.

3. A method in accordance with claim 1, wherein adjusting at least one of the radiation fields comprises adjusting a position of a radiator that generates one of the one or more radiation fields.

4. A method in accordance with claim 1, wherein adjusting at least one of the radiation fields comprises varying a power level of the radiation field.

5. A method in accordance with claim 1, wherein generating one or more radiation fields comprises generating a directional beam of radiation, and wherein adjusting at least one of the radiation fields comprises adjusting the direction of the directional beam of radiation.

6. A method in accordance with claim 1, wherein adjusting at least one of the radiation fields comprises adjusting said radiation field so as to maximize the intensity of radiation in the target area.

7. A method in accordance with claim 1, wherein generating one or more radiation fields comprises generating at least two radiation fields.

8. A method in accordance with claim 7, wherein adjusting at least one of the radiator fields comprises aiming the radiation fields commonly at the target area.

9. A method in accordance with claim 7, wherein generating one or more radiation fields comprises generating two radiation fields having a common frequency.

10. A method in accordance with any of claims 1-9, wherein measuring a physical parameter at the sensing portion of the probe comprises measuring the intensity of radiation thereat.

11. A method in accordance with any of claims 1-9, wherein providing a probe in the body comprises inserting the probe so that its sensing portion is located adjacent to the target area, and comprising determining a displacement of the sensing portion of the probe relative to the target area.

12. A method in accordance with claim 11, wherein adjusting at least one of the radiation fields comprises altering the adjustment in response to the displacement of the sensing portion of the probe from the target area.

13. A method in accordance with any of claims 1-9, wherein adjusting at least one of the radiation fields comprises dynamically adjusting the radiation field in response to a physiological motion.

14. A method in accordance with claim 13, wherein dynamically adjusting the radiation field in response to a physiological motion comprises cyclically varying the radiation field between two or more adjustment settings in response to a cyclical physiological motion.

15. A method in accordance with claim 14, wherein cyclically varying comprises applying irradiation substantially only at a portion of the cycle of the physiological motion.

16. A method in accordance with claim 14, and comprising receiving signals indicative of the physiological motion.

17. A method in accordance with claim 16, wherein receiving signals indicative of physiological motion comprises determining the position of the sensing portion of the probe.

18. A method in accordance with claim 17, wherein determining the position of the sensing portion of the probe comprises determining the position of the sensing portion of the probe relative to a reference position coupled to the body.

19. A method in accordance with claim 17, wherein determining the position of the sensing portion of the probe comprises determining the location of the sensing portion of the probe using a position sensor on the probe.

20. A method in accordance with claim 17, wherein determining the position of the sensing portion of the probe comprises determining the location of the sensing portion of the probe using an image of the probe.

21. A method in accordance with claim 17, wherein the radiation field tracks the position of the sensing portion of the probe.

22. A method in accordance with claim 17, comprising, determining the irradiation of tissues outside of the target area responsive to the relative positions of the probe and the radiators.

23. A method in accordance with claim 22, wherein adjusting at least one radiation field comprises adjusting at least one radiation field in response to the determined irradiation of tissues outside the target area.

24. A method in accordance with claim 17, wherein adjusting at least one radiation field comprises retrieving calibration data responsive to the probe position.

25. A method in accordance with claim 13, wherein dynamically adjusting the radiation field in response to a physiological motion comprises dynamically adjusting the radiation field in response to respiratory motion.

26. A method in accordance with claim 13, wherein dynamically adjusting the radiation field in response to a physiological motion comprises dynamically adjusting the radiation field in response to cardiac motion.

27. A method in accordance with claim 13, wherein dynamically adjusting the radiation field in response to a physiological motion comprises dynamically adjusting the radiation field in response to gastrointestinal motion.

28. A method in accordance with any of claims 1-9, wherein generating one or more radiation fields comprises generating a field of ultrasound radiation.

29. A method in accordance with any of claims 1-9, wherein generating one or more radiation fields comprises generating a field of electromagnetic radiation.

30. A method in accordance with any of claims 1-9, wherein measuring a physical parameter at the sensing portion of the probe comprises measuring a temperature thereat.

31. A method in accordance with claim 30, wherein adjusting at least one of the radiation fields comprises reducing a power level of at least one of the one or more radiation fields when a desired temperature is reached.

32. A method in accordance with claim 30, wherein adjusting at least one of the radiation fields comprises increasing a power level of a field of ionizing radiation when a desired temperature is reached.

33. A method in accordance with any of claims 1-9, wherein generating one or more radiation fields comprises generating a field of ionizing radiation.

34. A method in accordance with claim 33, wherein the ionizing radiation comprises x-ray radiation.

35. A method in accordance with claim 33, wherein measuring a physical parameter at the sensing portion of the probe comprises measuring a temperature thereat.

36. A method in accordance with claim 35, wherein adjusting at least one of the radiation fields comprises increasing a power level of the field of ionizing radiation when a desired temperature is reached.

37. A method in accordance with any of claims 1-9, and comprising injecting a therapeutic substance into the target area.

38. A method in accordance with claim 37, wherein injecting a therapeutic substance comprises injecting microbubbles.

39. A method in accordance with any of claims 1-9, wherein providing a probe, comprises:

inserting a probe into the body; and

maintaining the probe inside the body for at least two consecutive radiation therapy sessions.

40. A method of optimizing irradiation of a moving target area inside the body of a subject, comprising:

providing a probe inside the body, such that at least a sensing portion thereof is inside or adjacent to the moving target area;

generating one or more radiation fields in a vicinity of the moving target area;

determining a relative orientation between said fields and said probe; and

adjusting at least one of the radiation fields in response to said determined relative orientation.

41. A method according to claim 40, wherein adjusting at least one of the radiation fields comprises adjusting an intensity of the field.

42. Apparatus for irradiation of a target inside the body of a subject, comprising:

a probe, having a physical sensor at a sensing portion thereof, adapted to be inserted into the body to a position in or adjacent to the target;

a target motion sensor; and

one or more radiators, which generate energy fields in the body in the vicinity of the target including the position of the physical sensor,

wherein the physical sensor measures a physical parameter associated with the energy fields generated by the one or more radiators,

wherein at least one of the one or more radiators has one or more adjustable characteristics, and

wherein at least one of the one or more adjustable characteristics of at least one of the one or more radiators is adjusted in response to a signal generated by the physical sensor.

43. Apparatus in accordance with claim 42, wherein the signal from the sensor is transmitted from the probe using a wireless transmission method.

44. Apparatus in accordance with claim 42, wherein the physical sensor comprises an ultrasound transducer.

45. Apparatus in accordance with claim 42, wherein the physical sensor comprises an electromagnetic sensor.

46. Apparatus in accordance with claim 42, wherein the physical sensor comprises an ionizing radiation sensor.

47. Apparatus in accordance with claim 42, wherein the physical sensor comprises a temperature sensor.

48. Apparatus in accordance with claim 42, wherein the probe comprises a lumen, which is used to convey a therapeutic substance into the body.

49. Apparatus in accordance with claim 42, wherein the one or more adjustable characteristics comprise the position of the at least one radiator.

50. Apparatus in accordance with claim 42, wherein the one or more adjustable characteristics comprise the orientation of the at least one radiator.

51. Apparatus in accordance with claim 42, wherein the one or more adjustable characteristics comprise the power level of radiation generated by the at least one radiator.

52. Apparatus in accordance with claim 42, wherein at least one of the one or more radiators generates a directional beam of radiation, and

wherein the one or more adjustable characteristics comprise the direction of the directional beam of radiation generated by the radiator.

53. Apparatus in accordance with claim 52, wherein the radiators are movable relative to the target area.

54. Apparatus in accordance with claim 53, wherein the radiators are rotatable around the target area.

55. Apparatus in accordance with any of claims 42-52, wherein at least one of the one or more radiators generate a beam with a focal point and wherein the one or more adjustable characteristics comprises the location of the focal point.

56. Apparatus in accordance with claim 55, wherein the focal point is movable in three dimensions.

57. Apparatus in accordance with any of claims 42-52, and comprising a radiator controller, which adjusts at least one of the one or more adjustable characteristics automatically in response to signals transmitted from the probe.

58. Apparatus in accordance with claim 57, wherein the radiator controller adjusts the at least one adjustable characteristic dynamically, in response to motion of the target relative to the one or more radiators.

59. Apparatus in accordance with claim 58, wherein the target motion sensor generates signals indicative of physiological motion, which signals are received by the radiator controller.

60. Apparatus in accordance with claim 59, wherein the target motion sensor includes an imager which images the target area and an image processor which analyses the image to determine target movement.

61. Apparatus in accordance with claim 59, wherein the target motion sensor includes an abdominal belt which determines the breathing phase.

62. Apparatus in accordance with claim 59, wherein the target motion sensor includes a position sensor mounted on the probe.

63. Apparatus in accordance with any of claims 42-52, wherein the one or more radiators comprise an ultrasound radiator.

64. Apparatus in accordance with any of claims 42-52, wherein the one or more radiators comprise an electromagnetic radiator.

65. Apparatus in accordance with any of claims 42-52, wherein the one or more radiators comprise a phased array.

66. Apparatus in accordance with any of claims 42-52, wherein the one or more radiators comprise a source of ionizing radiation.

67. Apparatus in accordance with any of claims 42-52, wherein the one or more radiators comprise a mechanically steerable radiator.

68. A method of minimizing radiation damage to sensitive tissue during radiation therapy of a target tissue, comprising:

determining the position of a probe inserted in a first tissue portion, which first tissue portion has a positional relationship to the sensitive tissue, wherein the position is determined utilizing a position sensor mounted on the probe; and

determining an irradiation path from at least one radiator to the sensitive tissue responsive to the determined position and the positional relationship and responsive to an desired irradiation of the target tissue.

69. A method according to claim 68, comprising adjusting an output parameter of said at least one radiator responsive to said determined irradiation path.

70. A method according to claim 68, wherein said first tissue is in physiological motion.

71. A method according to claim 68, comprising moving said radiator relative to the first tissue.

72. A method according to any of claims 68-71, wherein said sensitive tissue has a known

positional relationship to the target tissue.

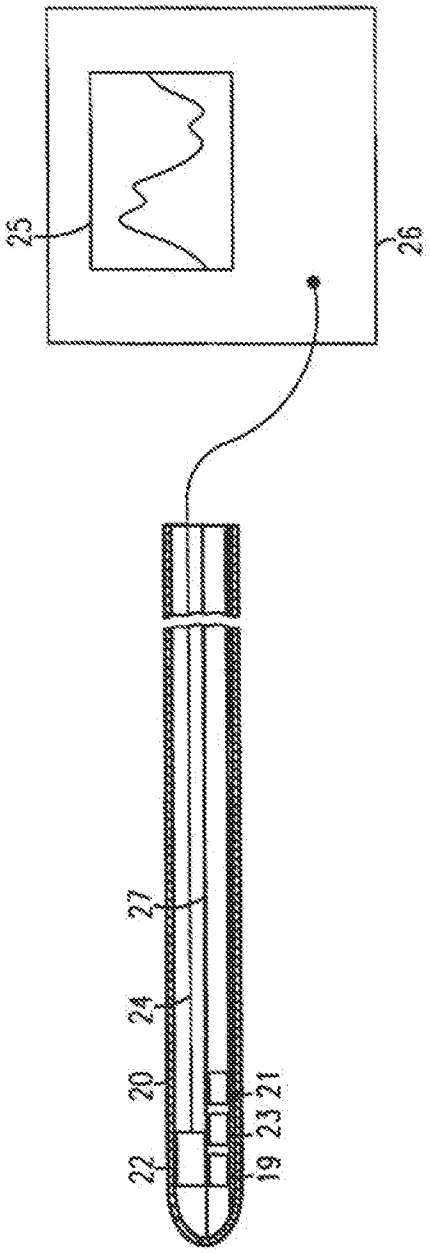

FIG. 1

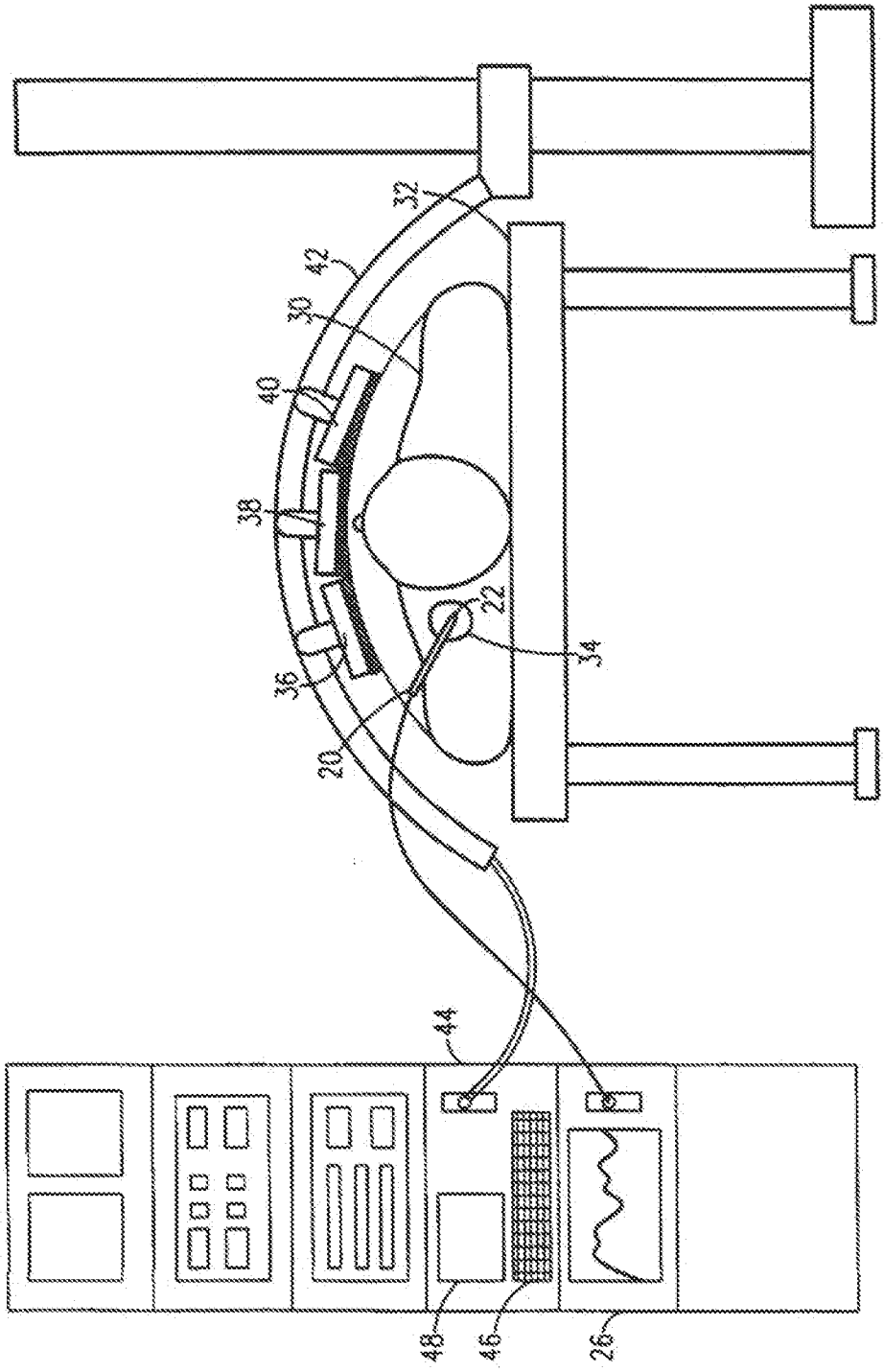

FIG. 2

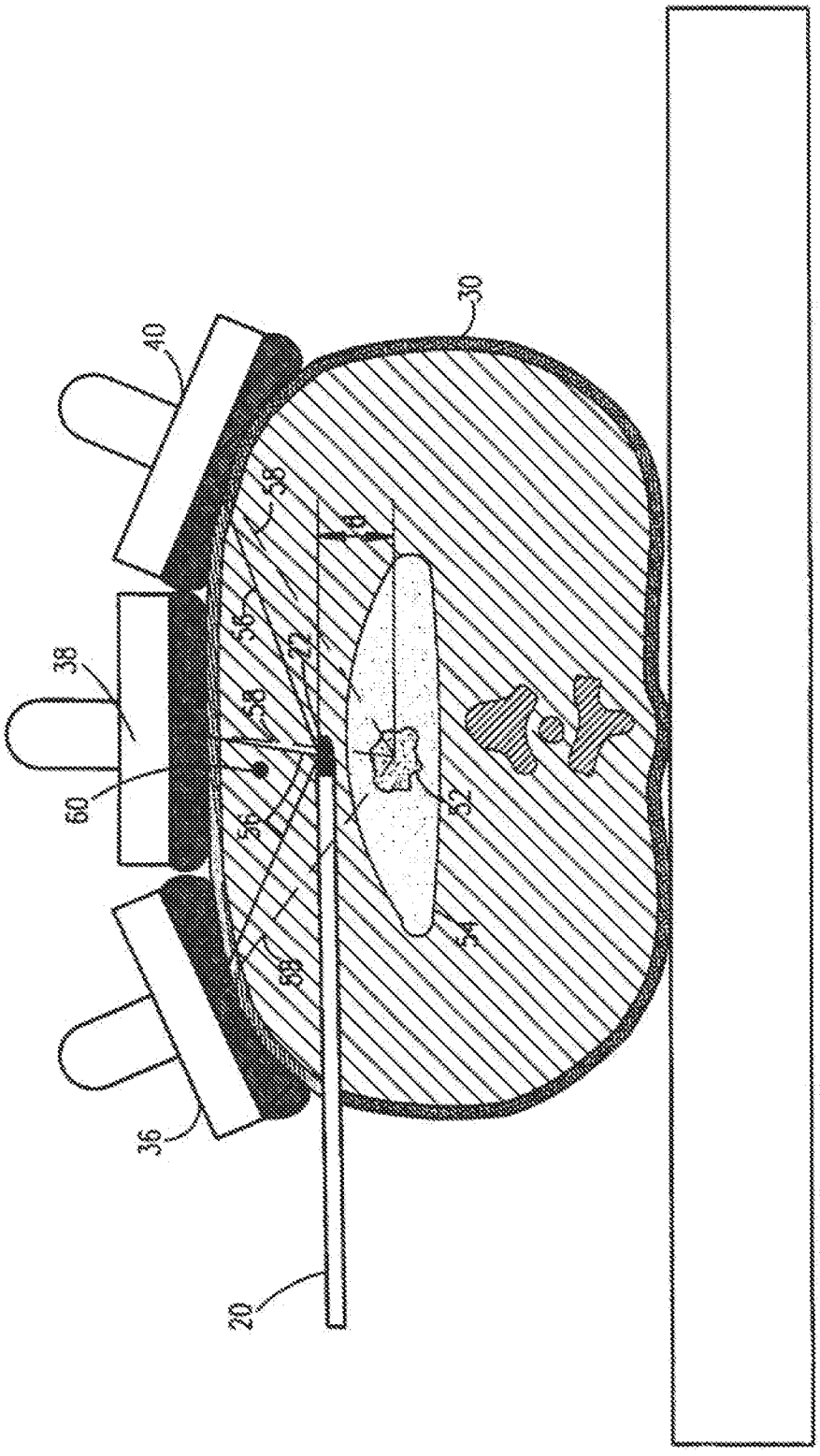

FIG. 3

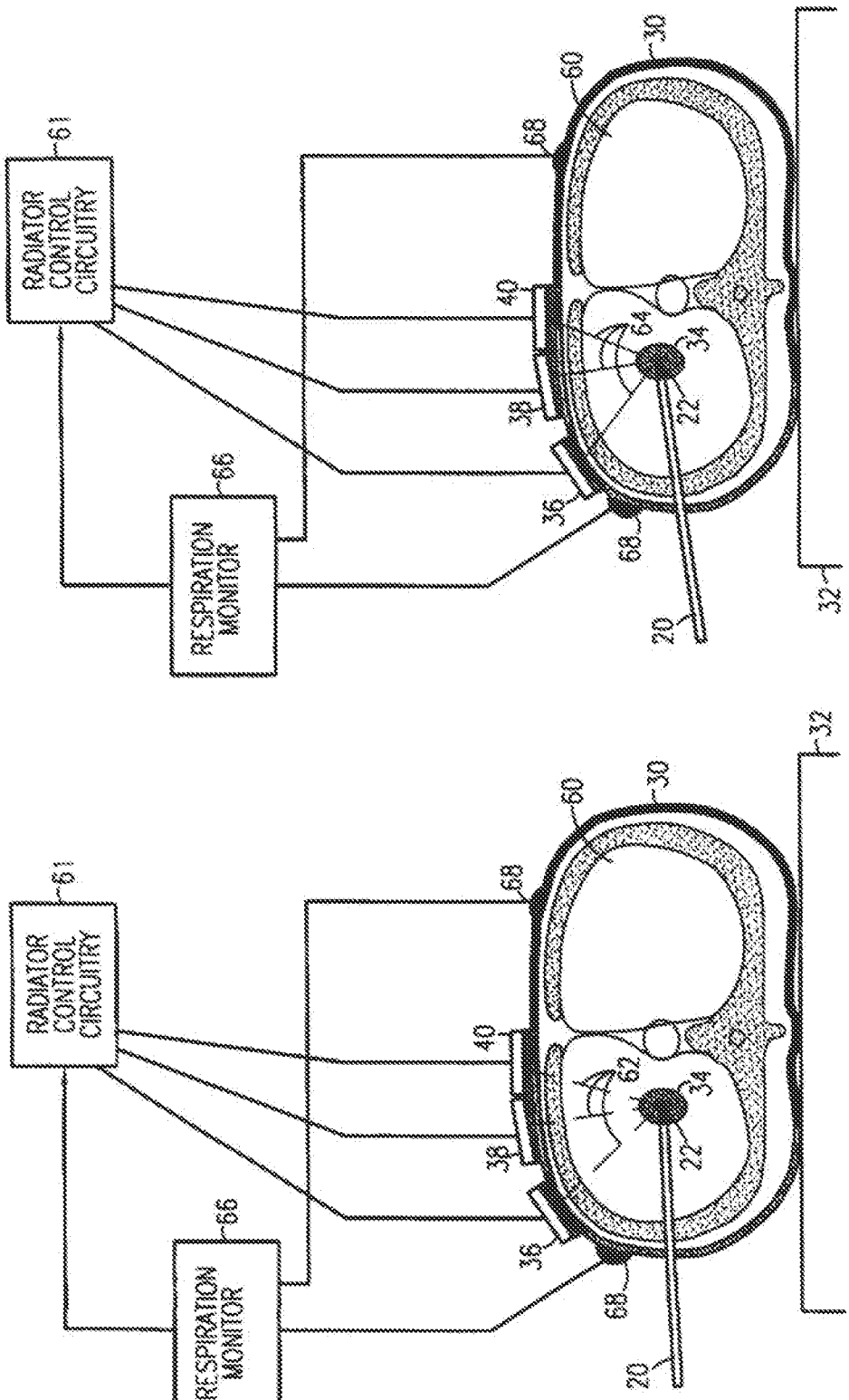
RADIATOR CONTROL CIRCUITRY
61
RESPIRATION MONITOR
66
68
60
30
40
38
36
64
34
22
20
32

FIG. 4B

RADIATOR CONTROL CIRCUITRY
61
RESPIRATION MONITOR
66
68
60
30
40
38
36
62
34
22
20
32

FIG. 4A

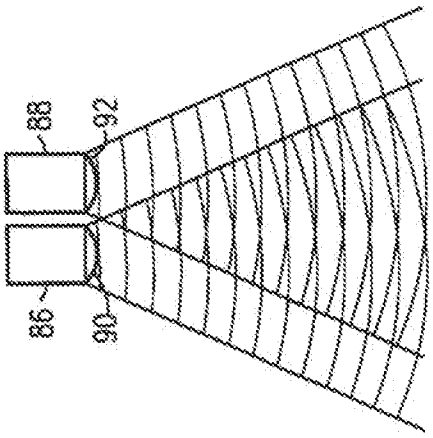

FIG. 5D

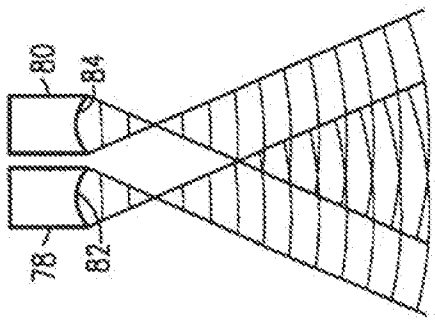

FIG. 5C

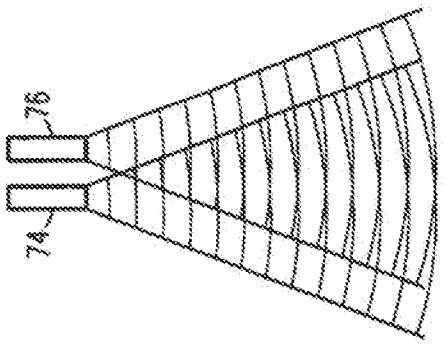

FIG. 5B

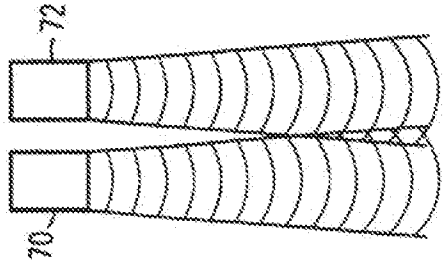

FIG. 5A

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL97/00056

A. CLASSIFICATION OF SUBJECT MATTER
(PC(6) : A61B 17/22
US CL. : 128/660.03,662.05
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 128/660.03,662.05

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
128/653.1,660.01,660.03,662.05,662.06;601/2, 3, 4; 607/97, 122, 378/162, 205

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 5,295,484 A (MARCUS ET AL) 22 March 1994, see entire document.	1-9, 11-24, 26, 28, 40-44, 49, 51-53, 68-72 25, 27, 45, 64, 65
X	US 4, 938, 217 A (LELE) 3 JULY 1990, see entire document	10
X	US 5, 377 678 A (DUMOULIN ET AL) 3 JANUARY 1995, see entire document	29
X, E	US 5, 606, 974 A (CASTELLANO ET AL) 4 MARCH 1997, see entire document	30, 31, 33 47

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 31 MAY 1997	Date of mailing of the international search report 23 JUN 1997
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ELENI MANTIS MERCADER Telephone No. (703)308-0858

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL97/00056

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5, 383, 455 A (HAGELAUER) 24 JANUARY 1995, see entire document	32, 33, 34, 35, 36, 46, 66
X	US 5, 078, 144 A (SEKINO ET AL) 7 JANUARY 1992, see entire document	37, 38, 39, 48
X,P	US 5,590,657 A (CAIN ET AL) 7 JANUARY 1997, see entire document	40, 41